IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Patrick G. Hogan et al.
Serial No. : Unassigned
Filed : Herewith
Title : SPECIFIC INHIBITORS OF NFAT ACTIVATION BY CALCINEURIN AND THEIR USE IN TREATING IMMUNE-RELATED DISEASES

BOX PATENT APPLICATION
Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the specification:

Replace the paragraph at page 1, lines 3 to 4, immediately after the title "Specific Inhibitors of NFAT Activation by Calcineurin and their Use in Treating Immune-Related Diseases," with the following rewritten paragraph:

--This application is a continuation of application serial number 09/248,620, filed February 11, 1999, which claims the benefit of U.S. Provisional Application No. 60/074,467, filed February 12, 1998 which are incorporated herein by reference in their entirety.--

Replace the paragraph beginning at page 5, line 10, with the following rewritten paragraph:

--Another aspect of the invention is an isolated polynucleotide encoding the peptide comprising the amino acid sequence as set forth in SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, or biologically active analogs thereof. Preferred polynucleotide

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Leroy Jenkins
Typed or Printed Name of Person Signing Certificate

sequences are, e.g., the sequences as set forth in SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, and SEQ ID NO:114.--

Replace the paragraph beginning at page 7, line 1, with the following rewritten paragraph:

--In preferred embodiments, the gene therapy vector comprises a nucleotide sequence encoding the peptide comprising the amino acid sequence as set forth in SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, or biologically active analogs thereof. In certain embodiments, the gene therapy vector comprises the nucleotide sequences as set forth in SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, or SEQ ID NO:114.--

Replace the paragraph beginning at page 30, line 18, with the following rewritten paragraph:

--The invention also includes an isolated polynucleotide encoding the peptide comprising the amino acid sequence as set forth in SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, or biologically active analogs thereof. Preferred polynucleotide sequences are, e.g., the sequences as set forth in SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, and SEQ ID NO:114.--

Replace the paragraph beginning at page 32, line 23, with the following rewritten paragraph:

--The coding sequence which encodes the peptide fragments can be identical to the coding sequences as set forth in SEQ ID NOS:36-70, 72, 83-92 or 109-114, or can be a different coding sequence, which coding sequence, as a result of the redundancy or degeneracy of the genetic code, encodes the same peptide fragments as the nucleic acid as set forth in SEQ ID NOS:36-70, 72, 83-92 or 109-114.--

Replace the paragraph beginning at page 33, line 19, with the following rewritten paragraph:

--In preferred embodiments, the gene therapy vector comprises a nucleotide sequence encoding the peptide comprising the amino acid sequence as set forth in SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, or biologically active analogs thereof. In certain embodiments, the gene therapy vector comprises the nucleotide sequences as set forth in SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, or SEQ ID NO:114. The invention also includes nucleotide sequences which are capable of hybridizing to and which are at least about 70%, preferably at least about 80%, more preferably yet at least about 85%, more preferably yet at least about 90%, more preferably yet at least about 95%, more preferably yet at least about 97%, and most preferably at least about 98% identical to these nucleotide sequences, and which encode a peptide having biological activity.--

Replace the paragraph beginning at page 39, line 12, with the following rewritten paragraph:

--In certain embodiments, the therapeutically effective amount of the peptide fragment is provided by providing to the animal a recombinant nucleic acid having a nucleotide sequence encoding the peptide fragment or a biologically active analog thereof, and which is capable of expressing the peptide fragment or biologically active analog thereof *in vivo*. The peptide fragment is administered to the animal by administering the recombinant nucleic acid. The nucleic acid can be, e.g., any of the polynucleotides described herein. Certain preferred nucleic acids are polynucleotides encoding the peptide comprising the amino acid sequence as set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or biologically active analogs thereof, e.g., the sequences as set forth in SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 and SEQ ID NO:39. Other preferred nucleic acids are polynucleotides encoding the peptide comprising the amino acid sequence as set forth in SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, or biologically active analogs thereof, e.g., the sequences as set forth in SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, and

SEQ ID NO:114. In certain embodiments, the recombinant nucleic acid is a gene therapy vector, e.g., as described herein.--

In the claims:

Please cancel claims 1 to 144.

Please add claims 145 to 164 as follows:

-- 145. An isolated polypeptide comprising a sequence of at least 6 amino acids but no more than 150 amino acids of the conserved regulatory domain of Nuclear Factor of Activated T-cell (NFAT) protein, wherein said at least six amino acids consists of SEQ ID NO:77, wherein X_1 is S or R, X_2 is E, R, or Q, and wherein X_3 is I or F.

146. The isolated polypeptide of claim 145, wherein said sequence of at least six amino acids is selected from the group consisting of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, and SEQ ID NO:71.

147. The polypeptide of claim 145, wherein said polypeptide comprises a sequence of at least 6 amino acid residues and less than 100 amino acid residues of the conserved regulatory domain of NFAT protein.

148. The polypeptide of claim 145, wherein said polypeptide comprises a sequence of at least 6 amino acid residues and less than 50 amino acid residues of the conserved regulatory domain of NFAT protein.

149. The polypeptide of claim 145, wherein said polypeptide comprises a sequence of at least 6 amino acid residues and less than 30 amino acid residues of the conserved regulatory domain of NFAT protein.

150. The polypeptide of claim 145, wherein said polypeptide comprises a sequence of at least 6 amino acid residues and less than 20 amino acid residues of the conserved regulatory domain of NFAT protein.

151. The polypeptide of claim 145, wherein said polypeptide comprises a sequence of at least 6 amino acid residues and less than 10 amino acid residues of the conserved regulatory domain of NFAT protein.

152. The polypeptide of claim 145, wherein said polypeptide comprises a sequence of 6 amino acid residues, and only 6 amino acid residues, of the conserved regulatory domain of NFAT protein, wherein said 6 amino acids consists of any one of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, and SEQ ID NO:71.

153. The polypeptide of claim 152, wherein said polypeptide inhibits protein-protein interaction between calcineurin and NFAT.

154. An isolated polypeptide consisting of any one of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, and SEQ ID NO:71.

155. The isolated polypeptide of claim 154, wherein said polypeptide inhibits protein-protein interaction between calcineurin and NFAT.

156. A fusion protein comprising the isolated polypeptide of claim 154 fused to at least one protein, wherein said at least one protein is other than an NFAT protein.

157. The fusion protein of claim 156, wherein said at least one protein comprises a maltose binding protein.

158. The fusion protein of claim 156, wherein said at least one protein comprises a glutathione S-transferase (GST) protein.

159. The fusion protein of claim 156 wherein said at least one protein comprises a green fluorescent protein, or a variant thereof.

160. The fusion protein of claim 156 wherein said at least one protein comprises a peptide tag.

161. The fusion protein of claim 156 wherein said at least one protein comprises thioredoxin.

162. The fusion protein of claim 156, wherein said at least one protein is fused to said isolated polypeptide at the N-terminus of said isolated polypeptide.

163. The fusion protein of claim 156, wherein said at least one protein is fused to said isolated polypeptide at the C-terminus of said isolated polypeptide.

164. The fusion protein of claim 162, further comprising a protein other than an NFAT protein fused to said isolated polypeptide at the C-terminus of said isolated polypeptide.--

REMARKS

Claims 145 to 164 are pending in this application. Applicants have cancelled claims 1 to 144, and added claims 145 to 164. The amendment results in a total of 20 claims. Support for such new claims can be found throughout the specification, e.g., at page 3, line 29, to page 4, line 4; page 20, line 23 to page 21, line 5; page 52, line 16, to page 53, line 9; and page 73, Example 2.

Applicants submit a paper copy and computer-readable copy of the Sequence Listing for the instant application. Amendments to the specification were made to renumber SEQ ID NOS: 110-115, as SEQ ID NOS:109-114, because these sequences were numbered incorrectly in the application as originally filed. Thus, these amendments add no new matter.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be examined and allowed. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 10861-004002.

Respectfully submitted,

Date: 1/31/02

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Version with markings to show changes made

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Paragraph beginning at page 7, line 1, has been amended as follows:

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e.g., the sequences as set forth in SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, and SEQ ID NO:114 [and SEQ ID NO:115].

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set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or biologically active analogs thereof, e.g., the sequences as set forth in SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 and SEQ ID NO:39. Other preferred nucleic acids are polynucleotides encoding the peptide comprising the amino acid sequence as set forth in SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, or biologically active analogs thereof, e.g., the sequences as set forth in SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, and SEQ ID NO:114 [and SEQ ID NO:115]. In certain embodiments, the recombinant nucleic acid is a gene therapy vector, e.g., as described herein.

In the claims:

Claims 1 to 144 have been cancelled.

Claims 145 to 164 have been added.